Anaphylaxis Guidelines

Dana V. Wallace, MD[a,*], Elham M. Hossny, MD, PhD[b], Michael Levin, MD, PhD[c], Daniel Munblit, MD, PhD[d,e], Paul J. Turner, FRACP, PhD[f]

KEYWORDS

• Anaphylaxis • Epinephrine • Adrenaline • Clinical guidelines • GRADE
• Diagnostic criteria • Epinephrine auto-injector • Emergency action plan

KEY POINTS

- *Methodological frameworks continue to evolve* away from consensus-based statements to provide more transparent, evidence-based, and patient-centered recommendations.
- *Definition and diagnostic criteria for anaphylaxis vary significantly*, especially in infants and patients without skin symptoms, contributing to inconsistent care and research outcomes.
- *While all guidelines universally recommend intramuscular epinephrine as first-line treatment* for anaphylaxis, epinephrine is underutilized by health care providers and patients. Adjunctive therapies such as corticosteroids and antihistamines lack evidence for acute management but are still commonly used before or in place of epinephrine.
- *Knowledge gaps among clinicians, parents, and educators* contribute to underdiagnosis and undertreatment, particularly in school and early care settings.
- *International harmonization of diagnostic tools and emergency plans* could improve patient outcomes and reduce disparities in anaphylaxis care.

INTRODUCTION

Clinical guidelines should base recommendations on the highest-quality evidence available to address clinically relevant questions regarding the diagnosis and

[a] Department of Medicine, Dr. Kiran C. Patel College of Allopathic Medicine, Nova Southeastern University, Fort Lauderdale, FL, USA; [b] Pediatric Allergy, Immunology and Rheumatology Division, Children's Hospital, Ain Shams University, Cairo, Egypt; [c] Department of Paediatric Allergology, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa; [d] Care for Long Term Conditions Division, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London, London, UK; [e] Department of Paediatrics and Paediatric Infectious Diseases, Institute of Child's Health, I.M. Sechenov First Moscow State Medical University, Sechenov University, Moscow, Russia; [f] Department of Paediatric Allergy and Immunology, National Heart & Lung Institute, Imperial College London, London, UK
* Corresponding author. 3535 S Ocean Drive, Suite 2806, Hollywood, FL 33019.
E-mail addresses: drdanawallace@gmail.com; dwallace@nova.edu

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Abbreviations	
ABC	Airway/Breathing/Circulation
ACE	Angiotensin-converting enzyme
AAAAI	American Academy of Allergy, Asthma, and Immunology
ACAAI	American College of Allergy, Asthma, and Immunology
AIT	Allergen immunotherapy
ASCIA	Australian Society of Clinical Immunology and Allergy
COI	Conflict of interest
CS	Corticosteroids (glucocorticosteroids)
CBS	Consensus-based statement
EAACI	European Academy of Allergy and Clinical Immunology
EAI	Epinephrine auto-injector
EAP	Emergency action plan
EtD	Evidence to Decision
FAAN	Food Allergy and Anaphylaxis Network
GA2LEN	Global Allergy and Asthma European Network, second phase
GRADE	Grading of Recommendations and Development of Evidence
IV	Intravenous
JSA	Japanese Society of Allergology
JTFPP	Joint Task Force on Practice Parameters
NIAID	National Institute of Allergy and Infectious Disease
NICE	National Institute of Health and Clinical Excellence (UK)
POA	Perioperative anaphylaxis
RCT	Randomized controlled trial
RCUK	Resuscitation Council UK
UK	United Kingdom
WAO	World Allergy Association

management of specific disease states, for example, anaphylaxis. Often, specific wording of recommendations is chosen to show the strength of the recommendation and the certainty of the supporting evidence. Clinicians are expected to take clinical practice guidelines into account, alongside the individual needs, preferences, and values of their patients, when making management decisions. Guidelines do not override the responsibility to make decisions appropriate to the circumstances of the individual, their families, and caregivers. Guidelines also inform practice standards that may be utilized by regulatory agencies and third-party payors and should be considered in the context of local and national priorities for funding and service development, respecting the need to eliminate unlawful discrimination and reduce health inequalities, such as access to care.

Given that anaphylaxis as a presentation does not differ in one country compared with another, harmonization of the various guidelines for anaphylaxis currently available is desirable, recognizing that adaptation to the local region will always be necessary. This article provides a comparison of the historical 2006 National Institute of Allergy and Infectious Diseases (NIAID)/Food Allergy & Anaphylaxis Network (FAAN) publication and 11 anaphylaxis guidelines developed or significantly updated from 2018 to 2025.[1–14] We have focused on guidelines developed in North America and other high-income countries, as well as major international organizations.

This article will compare and contrast the methodology used to develop anaphylaxis guidelines, the definitions and criteria used, areas of complete or nearly complete agreement, differences in anaphylaxis management (both subtle and significant), the assessment of risk, for example, for patients on beta-blockers, and remaining gaps in diagnosis and management.

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METHODOLOGICAL FRAMEWORKS FOR ANAPHYLAXIS GUIDELINES

We compare the methodologies used by contemporary anaphylaxis guidelines in **Table 1**, focusing on strategies for evidence retrieval, appraisal, formulation of recommendations, stakeholder engagement, and conflicts of interest. Increasingly, guideline development groups are adopting the Grading of Recommendations and Development of Evidence (GRADE) system to appraise evidence and address benefits, harms, and feasibility. Some groups combine GRADE with AGREE II, which evaluates guideline quality across domains such as clarity, stakeholder involvement, and editorial independence. GRADE-based guidelines also consider patient values, costs, feasibility, and equity.

The Evidence to Decision (EtD) framework (a GRADE component) is also used but in isolation does not constitute full GRADE implementation. When evidence is insufficient, guidelines often rely on consensus-based statements (CBSs),[2–5] using threshold agreement or voting. This hybrid model is common due to the limited availability of randomized controlled trials (RCTs) in anaphylaxis, and therefore the need for lower-quality, other evidence sources, or even expert opinion.[3]

Framework choice and formulation of recommendations often reflect scope, resources, update needs, organizational mandates, and intended implementation. *De novo* guidelines favor GRADE, while updates may adopt GRADE-ADOLOPMENT[6] or consensus approaches. GRADE classifies evidence certainty from high to very low, while other evidence-grading systems use national classification structures or domain-specific levels.[2,4,5,9] The predominance of high-certainty evidence supports a strong recommendation. In contrast, low-certainty evidence leads to conditional recommendations and often necessitates expert consensus, ideally incorporating a minimum voting threshold for agreement.

Guideline panels should, ideally, include multidisciplinary clinicians, patient representatives, and methodologists, ensuring that recommendations are practical and patient-centered.[3,4] Conflict of interest (COI) policies include mandatory disclosures and the exclusion of conflicted members from decision-making,[2,3] a process that is critical for credibility and transparency. Most guidelines undergo external review via independent reviewers, international, national, and/or regional societies, health ministries, and/or the public.

Although the specific methodological frameworks of the 12 guidelines reviewed here vary, there is a clear trend toward more evidence-based, expert-informed recommendations developed in a structured and inclusive process. The increasing inclusion of diverse stakeholders, for example, people with lived experience and a broader spectrum of health care professionals, contributes to the creation of more patient-centered, relevant, and practically implementable guidelines.

For end users, an understanding of the underlying methodological approaches is essential for appropriately interpreting recommendations and applying them in clinical practice. The low certainty of evidence for most recommendations highlights the pressing need for better quality primary research in anaphylaxis. The variation in methods reflects the practical constraints and differing resources available to guideline developers, but emphasizes the need to achieve international harmonization of best practice recommendations.

ANAPHYLAXIS DEFINITION AND CRITERIA

To address the historical inconsistencies in the diagnosis of anaphylaxis, the NIAID and the FAAN published in 2006 a consensus-based definition and clinical criteria which have been widely adopted for use in clinical care and research.[16] Anaphylaxis

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Table 1
Comparison of methodologies used in anaphylaxis guideline development

Guideline Name/ Issuing Body	Publication/ Update Year	Stated Methodological Framework	Evidence Gathering Processes[a]	Evidence Grading System (If Specified)	Recommendation Development[a]	Stakeholder Involvement	Peer Review Process	Conflict of Interest Management
NICE Quality Standard QS119 (Derived from NICE CG134)[7–9]	2016 (QS119), Last updated 2024. CG134: 2011, updated 2020.	NICE guideline methodology (for CG134); Quality standard development process.	Systematic reviews, evidence appraisal, economic evaluations (for CG134).	NICE evidence statements, grading of recommendations (for CG134).	Guideline Development Group, consensus, stakeholder consultation (for CG134).	Clinical experts, patient/ carer representatives, public health, commissioners (for CG134).	Stakeholder consultation on draft guideline and quality standard.	NICE COI policy.
Resuscitation Council UK[6]	2021	GRADE-ADOLOPMENT	Review of previous guideline, new international evidence-based guidelines, database of FAQs. EtD tables published.	GRADE with EtD frameworks.	Executive Committee appointed co-chairs, Working Group, Consultation Panel feedback, public comment review.	Working Group (clinicians), Consultation Panel, public submissions.	Evidence tables/ conclusions peer-reviewed and published. Public consultation on draft.	Declared for Working Group members.
WAO Anaphylaxis Guidance[10]	2020	Consensus-based, informed by best available evidence (eg, SRs from other guidelines).	Based on previous guidelines, systematic reviews informing other guidelines.	Not explicitly detailed for all statements, but references GRADE analysis in a related parameter update.	WAO Anaphylaxis Committee compiled draft, refined via correspondence/ meetings, WAO Board review, WAO member society review/voting	WAO Anaphylaxis Committee, WAO Board, WAO member societies (national, regional, affiliate allergy societies).	Formal review by WAO member societies.	Detailed COI disclosures for each author.
Russian 'Анафилактический шок' (Anaphylactic Shock) Clinical Recommendation[5]	2025 (Approval year)	Systematic updates	Systematic search (PubMed, Cochrane, eLIBRARY, EMBASE, trial registries) by 2 members; 116 publications selected from 262	УДД (Level of Evidence Reliability) scales for diagnostic, prophylactic, therapeutic, rehab methods (1–5). УУР (Level of Conviction of Recommendations scales (A, B, C).	Independent thesis-recommendation formulation by 2 experts, then full working group discussion and consensus.	Working Group (allergists, clinical immunologists, anesthesiologists-resuscitators). Target audience: 36 medical specialties.	Approved at meeting of scientific-practical council of Ministry of Health.	Not explicitly detailed.
JTFPP (ACAAI/AAAAI) Anaphylaxis Practice Parameter Update[2]	2023	Primarily Consensus-Based Statements for this update; the previous 2020 update used GRADE. Terminology aims for consistency with GRADE but not full GRADE rigor for all CBSs.	Literature searches (PubMed, MEDLINE, Google Scholar, Cochrane), primarily 2015–2022. Observational studies, case series, lab reports, expert reviews used due to the few RCTs.	Strength of Recommendation (Strong/Conditional), Certainty of Evidence (High/Moderate/Low/ Very Low) for CBSs, based on evidence and expert opinion	JTFPP appointed Workgroup, developed key questions, literature review, drafting by sub-groups, full workgroup review/ revision, JTFPP review/ revision. Recommendations reflect majority opinion	JTFPP, Workgroup (experts), ACAAI/ AAAAI leadership, invited expert reviewers, general membership/public for comment.	JTFPP review, external expert review, public/ membership comment.	Standard COI disclosure, revision for bias, recusal from voting for conflicted members.

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EAACI Guidelines: Anaphylaxis Update[3]	2021 (Published 2022)	AGREE II framework, GRADE approach.	Systematic review by independent methodologists (GRADE Pro GDT). Comparative studies, prospective case series (for diagnosis/ epinephrine). Continuous evidence tracking.	Certainty of evidence (High, Moderate, Low, Very Low) based on GRADE.	TF used GRADE to formulate recommendations, evaluating problem importance, effects, evidence certainty, values, resource use, equity, etc. 80% consensus threshold	EAACI TF (9 countries: allergists, pediatricians, primary care, immunologists, emergency physicians, anesthetists, dieticians, nurses, psychologist, education, patient organizations). Methodologists.	External peer review by invited experts. Public consultation on EAACI Web site.	COIs declared; conflicted members not involved in final decisions for relevant recommendations. Independent methodologists. Funded by EAACI (no influence on content).
ASCIA Guidelines: Acute Management of Anaphylaxis[15]	2024 (Updated)	Based on published literature and expert review; consistent with other major guidelines.	Published literature, expert review. Aligned with WAO, AAAAI (GRADE), ACSQHC, ILCOR/ANZCOR.	Not explicitly detailed, but informed by guidelines using GRADE	Expert review. Consultation with ACSQHC, A&AA, NAS for related Clinical Care Standard.	ASCIA members (clinical immunology/allergy specialists). Consultation with A&AA, NAS for the related standard.	Not explicitly detailed in these guidelines but implies expert review.	Stated as "not influenced by commercial organizations."
Japanese Society of Allergology Anaphylaxis Guidelines[12]	2022 (2nd print 2023)	Consensus-based.	Literature review, referencing international guidelines (eg, WAO 2020), national surveys/ reports (MEXT, MHLW, JADER, JRC), academic publications.	"Recommendation Level C" defined for some treatments (based on non-experimental descriptive studies or analogy from RCTs).	Developed by Anaphylaxis Countermeasures Committee (expert working group).	Anaphylaxis Countermeasures Committee (clinicians from various specialties), creation cooperators. Target audience: physicians.	Not explicitly mentioned.	COIs disclosed on JSA website.
German Guideline (S2k) on acute therapy and management of anaphylaxis: 2021 update[4]	2021 (update to the 2014 version)	S2k consensus-based guideline. The process involves a systematic literature search combined with an informal consensus-finding process among experts.	A systematic search of literature in the MEDLINE and Cochrane Library databases published since the previous 2014 version. Due to the limited number of high-quality studies, the guideline also relies on case series, case reports, and experimental investigations	No formal evidence grading system (like GRADE) was used. This was due to the overall low level of scientifically reliable evidence available for anaphylaxis management	Recommendations were developed through an informal consensus-finding process, which included multiple telephone conferences and email-based voting procedures among the working group members	A multidisciplinary panel was involved, including experts from anesthesiology, dermatology, pediatrics, pharmacology, and emergency medicine. A patient organization, the German Allergy and Asthma Association, was also a key participant	The guideline was reviewed by the boards of all participating professional societies and submitted to the Association of the Scientific Medical Societies in Germany for review	Conflicts of interest were collected by the AWMF and evaluated by the guideline coordinator. The document states that the "guideline was produced without the influence or support of industry"

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Table 1
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Guideline Name/ Issuing Body	Publication/ Update Year	Stated Methodological Framework	Evidence Gathering Processes[a]	Evidence Grading System (If Specified)	Recommendation Development[a]	Stakeholder Involvement	Peer Review Process	Conflict of Interest Management
Canada 2018[14]	2018 reaffirmed 2011 guideline	Consensus-based position statement	Not specified	Not specified	Acute Care Committee of Canadian Pediatric Society	6-member Acute Care Committee	Reviewed by Canadian Pediatric Society's Allergy Section and Community Pediatrics Committee	Not specified
GA2LEN 2025[13]	2025 (journal publication)	Modified Delphi consensus methodology (≥80% agreement threshold)	Draft definition, overview and support tool written by a 12-member writing group; Iterative input from a 46-member international expert panel; 2 panel tele-conferences, surveys, and written comments	Not specified. No formal evidence-grading approach.	Three-round maximum anonymous Delphi surveys; consensus threshold ≥80% of respondents "agree/ strongly agree"	46 experts from 14 countries 31 professional organizations and 15 patient groups consulted; regulators provided feedback	Internal peer review through the Delphi rounds plus external endorsement	Full funding statement and detailed individual author disclosures provided
NIAID/FAAN 2006[16]	2006	No formal framework is described. Expert-consensus symposium report convened by NIAID and the Food Allergy & Anaphylaxis Network	Evidence consisted of presentations, literature overviews, and the collective clinical experience of the 35+ experts attending the 2-day meeting. Developed "largely on the basis of clinical experience"	Not reported. No formal evidence-grading approach.	Recommendations were produced through in-meeting discussion and consensus among the multidisciplinary participants; draft criteria were revised in open session until agreement was reached	Representatives from at least 16 professional societies, government bodies, and patient organizations contributed	Not explicitly mentioned	Not reported

[a] Key features outlined.

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was defined as "a serious allergic reaction that is rapid in onset and may cause death," which stressed the serious nature of the condition and provided conceptual clarity. The risk-based clinical criteria were intended to support clinicians to make a real-time diagnosis and help researchers with case identification (**Box 1**). **Table 2** provides a summary of the verbatim definitions of anaphylaxis used by all 12 guidelines.

While the NIAID/FAAN definition and clinical criteria have been incorporated into some guidelines, in some countries such as the United Kingdom[7–9,17] and Australia,[11,15] other criteria have been used, typically based on the Airway/Breathing/Circulation (ABC) approach. There has also been discord over the combination of gastrointestinal and skin features being considered as anaphylaxis when due to a food trigger.[18] As a result, in 2020, the World Allergy Organization (WAO), who had previously adopted the NIAID/FAAN definition and criteria, moved to modified approach incorporating both the NIAID/FAAN and other definitions.[10] The new WAO approach reduced the number of criteria from 3 to 2, modified the gastrointestinal criterion to better align with the approach used in the United Kingdom/Australia, and incorporated isolated respiratory involvement after exposure to a known or highly probable allergen (excluding inhalant allergens) as a likely indication of anaphylaxis. The WAO guideline was endorsed by over 50 national societies across the globe, including the American College of Allergy Asthma and Immunology (ACAAI). The 2021 Resuscitation Council UK (RCUK) definition was similar to the WAO 2020 approach, with an emphasis on an ABC approach for diagnosis.[6] The 2023 Japanese Society of Allergy (JSA) definition and the 2024 update from the Australasian Society of Clinical Immunology and Allergy are aligned with the WAO 2020 approach.[11,12]

The European Academy of Allergy and Clinical Immunology (EAACI) published an updated guideline in 2022, which still was based on the NIAID/FAAN 2006 framework, but also emphasized a greater need for health care professional recognition and management of anaphylaxis.[17]

Box 1
The NIAID/FAAN diagnostic criteria for anaphylaxis[16]

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus, flushing, swollen lips/tongue/uvula), and at least one of the following:
   - Respiratory compromise (eg, dyspnea, wheeze/bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)
   - Reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia, syncope, incontinence)
2. Two or more of the following occurring rapidly after exposure to a likely allergen (minutes to several hours):
   - Involvement of the skin-mucosal tissue (eg, generalized hives, pruritus, flushing, swollen lips/tongue/uvula)
   - Respiratory compromise (eg, dyspnea, wheeze/bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)
   - Reduced blood pressure or associated symptoms (eg, hypotonia, syncope, incontinence)
   - Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)
3. Reduced blood pressure after exposure to a known allergen for that patient (minutes to several hours):
   - Infants and children: Low systolic BP (age-specific) or greater than 30% decrease in systolic BP
   - Adults: Systolic BP less than 90 mm Hg or greater than 30% decrease from baseline

Note: Fulfilling any one of the following 3 scenarios establishes a diagnosis of anaphylaxis.

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Table 2
Definition of anaphylaxis

Guideline Development Group	Verbatim Definition Used in Guideline
NIAID	A serious allergic reaction that is rapid in onset and may cause death
NICE	A severe, life-threatening, generalized or systemic hypersensitivity reaction. It is characterized by rapidly developing, life-threatening problems involving: the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and mucosal changes.
WAO	A serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterized by potentially life-threatening compromise in the airway, breathing, and/or the circulation, and may occur without typical skin features or circulatory shock being present.
RCUK	A serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. It is characterized by: sudden onset and rapid progression of symptoms; airway and/or breathing and/or circulation problems; usually, skin and/or mucosal changes (urticaria, flushing, or angioedema); these may be subtle or absent in 10%–20% of reactions.
Russian	Anaphylaxis is a life-threatening systemic immediate-type hypersensitivity reaction. It is characterized by the rapid onset of potentially life-threatening hemodynamic changes and/or respiratory system impairments. In addition to disturbances of the respiratory and circulatory systems, involvement of the skin, mucous membranes, and gastrointestinal tract may also occur.
JTFPP	A serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death.
EAACI	Anaphylaxis is a clinical emergency that all health care professionals need to be able to recognize and manage.
ASCIA	Any acute onset illness with typical skin features (urticarial rash or erythema/flushing, and/or angioedema), plus involvement of respiratory and/or cardiovascular/or persistent severe gastrointestinal symptoms; or any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present.
JSA	Anaphylaxis is a hypersensitivity reaction caused by the entry of an allergen or similar trigger, inducing systemic allergic symptoms across multiple organ systems and potentially posing a life-threatening risk.
German 52K	Anaphylaxis is a serious allergic (hypersensitivity) reaction that can progress rapidly and may cause death. It may involve the skin/mucosa (includes lip/tongue), respiratory (lungs, breathing), cardiovascular (heart, blood pressure), and/or gastrointestinal (stomach/gut) systems. Life-threatening anaphylaxis is characterized by respiratory and/or cardiovascular involvement and may occur without skin/mucosa involvement.
Canadian (2011, 2022)	2011 A severe, acute, and potentially life-threatening medical condition caused by the systemic release of mediators from mast cells and basophils.

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Table 2
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Guideline Development Group	Verbatim Definition Used in Guideline
	2022 Vaccine anaphylaxis definition: A severe systemic hypersensitivity reaction that represents the most severe form of allergic response and requires appropriate initial management by all medical professionals.
GA2LEN 2025	Anaphylaxis is a rare serious allergic (hypersensitivity) reaction that can progress rapidly and may cause death. It may involve the skin/mucosa (includes lip/tongue) respiratory (lungs, breathing), cardiovascular (heart, blood pressure), and/or gastrointestinal (stomach/gut) systems. Life-threatening anaphylaxis is characterized by respiratory and/or cardiovascular involvement and may occur without skin/mucosa involvement.

The Canadian Pediatric Society Anaphylaxis Working Group's guideline on anaphylaxis in infants and children, initially published in 2011 and reaffirmed in 2018, defined anaphylaxis similar to that of the NIAID, including that anaphylaxis is "caused by the systemic release of mediators from mast cells and basophils."[14]

The 2023 Joint Task Force on Practice Parameters (JTFPP) on Anaphylaxis (a collaboration between ACAAI and AAAAI) used the NIAID definition but added "usually" before "rapid onset."[2]

In 2025, the ANACARE consortium within the Global Allergy and Asthma Excellence Network (GA2LEN) used a Delphi consensus approach with an international expert panel to try to address discordance between the different definitions of anaphylaxis used.[13] The result was a modified definition based on a hybrid of the 2006 NIAID/FAAN and 2020 WAO documents. The GA2LEN also included a clinical support tool to help determine the presence of anaphylaxis.

Table 3 compares the number of anaphylaxis criteria required and the variation of each criterion that 11 subsequent international guidelines have used to establish the presence of anaphylaxis.

ANAPHYLAXIS MANAGEMENT: AGREEMENT ACROSS INTERNATIONAL GUIDELINES

The 12 guidelines reviewed in this article are generally in agreement with the principal management strategies and the order in which they should be implemented (**Table 4**). Clinical guidelines universally emphasize the importance of prompt diagnosis, which typically involves multiple organ systems. However, isolated but rather severe symptoms such as hypotension or bronchospasm following exposure to a known or likely allergen also represent key diagnostic presentations. Variations in criteria are generally aimed at improving diagnostic sensitivity and specificity for clinical or research use, rather than reflecting fundamental disagreement on the nature of anaphylaxis. This shared diagnostic foundation supports timely intervention, which is critical in managing anaphylactic emergencies.

There is broad consensus on (1) removing the suspected trigger (2) calling for emergency medical help and positioning the patient appropriately. The default position is supine, with legs elevated; if respiratory distress is present, a position that supports breathing, such as sitting upright, may be more appropriate. For pregnant individuals, a left lateral position is recommended.

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Table 3
Guideline comparison of criteria, symptoms, timing, and tryptase use

Aspect	NIAID/FAAN 2006[16]	EAACI 2022[3]	NICE 2011, 2016, 2024[7–9]	WAO 2020[10]	RCUK 2021[6]	Canada 2018; 2022[14,19]	JTFPP 2023[2]	ASCIA 2024[11]	GA2LEN 2025[13]	Russian 2025[5]	Japan (JSA) 2022[12]	Guideline (S2k) 2021[4]
Number of criteria	3	3	No formal numbered set is provided	2	No numbered list, but a recognition triad: (1) sudden onset/rapid progression, (2) Airway and/or Breathing and/or Circulation problems, and (3) usually skin/mucosal changes.	3	3	2 (adapted from the WAO 2020 consensus)	3	3	2	3
Organ System Involvement	Criteria 1 and 2 require 2 systems' involvement.	Criteria 1 and 2 require 2 systems' involvement.	Not defined	Four systems are named: skin/mucosa, respiratory, cardiovascular, and gastrointestinal. Criterion 1 pairs skin/mucosa + ≥ 1 other system; Criterion 2 focuses on respiratory and/or cardiovascular compromise	Allows diagnosis based on airway/breathing/circulation without skin symptoms.	Similar to JTFPP but adapted for pediatric cases.	Criteria 1 and 2 require 2 systems' involvement	Requires ≥2 systems or hypotension or bronchospasm or Upper respiratory obstruction alone when anaphylaxis is considered possible.	Skin/mucosa, respiratory, cardiovascular, and gastrointestinal. The criteria require different combinations of these systems according to the likelihood of allergen exposure.	Skin/mucosa, respiratory (airway + breathing), cardiovascular (circulation/blood pressure), and gastrointestinal systems; the first 2 criteria combine ≥2 of these, always including respiratory and/or circulatory compromise	Criterion 1 requires skin/mucosal symptoms plus at least one other organ system (respiratory, cardiovascular, or gastrointestinal). Criterion 2 allows for diagnosis with single-system involvement (circulatory or respiratory) after exposure to a known allergen	Skin/mucosa, respiratory tract, cardiovascular system, and gastrointestinal tract can feature: (1) skin + respiratory and/or circulatory compromise; (2) any ≥2 of the 4 systems after a likely allergen; (3) isolated cardiovascular compromise (hypotension)
Single system criteria	Hypotension	Hypotension	One ABC sign alone is enough to trigger EAI use; multi-system involvement is not required.	Hypotension or Bronchospasm or laryngeal involvement	may present with either an Airway, Breathing, or Circulation problem (any one) and still meet the definition, even if no other systems are involved.	Hypotension	WAO criterion 2 (and NIAID criterion 3) lets isolated hypotension, isolated bronchospasm, or isolated laryngeal involvement qualify when the trigger is known/highly probable.	Criterion 2 permits isolated hypotension or bronchospasm or laryngeal involvement after exposure to a known/highly probable allergen, even when skin features are absent.	Criterion 3 accepts isolated respiratory or isolated cardiovascular compromise after exposure to a known allergen.	hypotension after exposure to a known allergen	Hypotension, bronchospasm, or laryngeal symptoms alone are sufficient for diagnosis after exposure to a known or highly probable allergen.	Hypotension after exposure to a known allergen fulfills Criterion 3

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Role of Skin Symptoms	Mandatory in Criterion 1, optional in Criterion 2, and not required in Criterion 3	Emphasizes skin involvement for ≥2 systems.	"Usually present"	Skin/mucosa involvement common but not mandatory.	Skin symptoms not required.	Includes skin but accounts for pediatric presentations without it.	Skin symptoms included but not mandatory.	Not required when hypotension or bronchospasm present or upper airway obstruction	Skin/mucosal signs are obligatory in Criterion 1, optional in Criterion 2, and absent in Criterion 3; thus, they are common but not indispensable for diagnosis	Skin/mucosal signs are required in Criterion 1, optional in Criterion 2, and absent in Criterion 3; common but not mandatory for diagnosis.	Skin/mucosal symptoms are required for the first diagnostic criterion, but are not required for the second criterion if there is exposure to a known allergen	Skin/mucosal signs are obligatory in Criterion 1, optional in Criterion 2, and absent in Criterion 3; overall, they are common but not essential for diagnosis
Time Frame for Symptoms	Minutes to several hours	Onset within minutes to hours.	Rapidly developing, no time limits indicated	Acute onset emphasized broadly.	Acute onset, no strict time frame.	Acute onset highlighted.	Acute onset without strict limits.	Minutes to several hours	Acute presentation that can "progress rapidly", without assigning a strict minute-or-hour threshold	Minutes to several hours. Most reactions developing within 2 h (often ≤ 30 min for food, even faster for parenteral drugs or insect venom).	Symptoms must appear rapidly, within a time frame of minutes to several hours.	Acute sudden onset; symptoms usually within minutes and may progress rapidly, though delayed presentations[20]
Use of Tryptase	Can confirm mast-cell activation, but is positive in only ~21% of ED cases.	Encouraged for confirmation.	Obtain multiple acute and timed samples in all patients ≥ 16 y of age with suspected anaphylaxis	Obtain peak at 15 min-3 hrs.; baseline ≥ 24 h later	Obtain when dx is uncertain; peak within 2 h or at least by 6–8 h; obtain convalescent baseline.	Not discussed	Obtain as soon as possible; measure baseline in recurrent, idiopathic, or severe anaphylaxis	Not discussed	Tryptase measurement can be helpful—when feasible—to corroborate the diagnosis later, but a normal value does not exclude anaphylaxis	Serum tryptase 15 min–3 h after first symptoms and again after recovery to aid differential diagnosis; a normal level does not rule out anaphylaxis	A normal tryptase level does not rule out anaphylaxis. If measured, it is recommended to compare a sample taken 15 min to 3 h after symptom onset with a baseline value.	1–3 h after onset and again at baseline to support (but not rule out) the diagnosis

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Table 4
Summary of recommendations in anaphylaxis management

Aspect of Management	Agreed Recommendation/Principle	Supporting Guidelines[a]
Recognition	Rapid clinical diagnosis based on acute onset of characteristic signs and symptoms, often multi-systemic but can be isolated severe reactions to known allergen.	WAO, RCUK, ASCIA, JSA, German, Russian, ACAAI/AAAAI, EAACI
Initial actions	Remove trigger (if possible), call for emergency medical help, appropriate patient positioning (supine/left lateral for pregnancy).	RCUK, WAO, ASCIA, German, ASBAI, EAACI
First-line treatment	Epinephrine [adrenaline] is the first-line, life-saving treatment.	NICE, RCUK, WAO, ASCIA, JSA, German, Russian, ACAAI/AAAAI, EAACI, ASBAI
Epinephrine route	Intramuscular (IM) injection into the anterolateral thigh is the preferred initial route.	RCUK, WAO, ASCIA, JSA, German, Russian, ACAAI/AAAAI, EAACI, ASBAI
Epinephrine dosage (IM)	Weight-based (0.01 mg/kg), typically up to 0.5 mg for adults and 0.15–0.3 mg for children, using 1:1000 (1 mg/mL) solution.	RCUK, WAO, ASCIA, JSA, German, Russian, ACAAI/AAAAI, EAACI, ASBAI
Repeat epinephrine dose	Repeat IM epinephrine dose every 5–15 min if symptoms persist or worsen.	RCUK, WAO, ASCIA, JSA, German, Russian, EAACI, ASBAI
Oxygen	Administer high-flow oxygen.	RCUK, WAO, ASCIA, German, ASBAI, EAACI
Intravenous fluids	Administer IV crystalloid fluids for hypotension/shock, especially if refractory to epinephrine.	RCUK, WAO, ASCIA, JSA, German, Russian, ACAAI/AAAAI, EAACI, ASBAI
Nebulized bronchodilators	Consider for persistent bronchospasm after epinephrine; not a substitute for epinephrine.	RCUK, WAO, ASCIA, JSA, German, Russian, EAACI, ASBAI
Glucagon	Consider for patients on beta-blockers refractory to epinephrine.	RCUK, WAO, ASCIA, JSA, German, ASBAI
Antihistamines & corticosteroids	Second-line/adjunctive; not first-line life-saving treatment and must not delay epinephrine.	RCUK, WAO, German, ASBAI, EAACI, JSA
Biphasic reactions	Recognize possibility and observe patient post-resolution (duration often risk-stratified).	RCUK, WAO, ASCIA, JSA, German, ACAAI/AAAAI, EAACI, ASBAI
Patient education	Comprehensive education on trigger avoidance, symptom recognition, AAI use, emergency action plan.	NICE, RCUK, WAO, ASCIA, JSA, German, Russian, ACAAI/AAAAI, EAACI, ASBAI

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Table 4
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Aspect of Management	Agreed Recommendation/Principle	Supporting Guidelines[a]
Epinephrine auto-injectors (EAIs)	Prescribe to patients at ongoing risk and provide training in their use. Many recommend 2 EAIs.	NICE, RCUK, WAO, ASCIA, JSA, German, ACAAI/ AAAAI, EAACI, ASBAI
Specialist referral	Refer to an allergy specialist for diagnosis, trigger identification, and long-term management.	NICE, RCUK, WAO, ASCIA, German, ASBAI, EAACI

[a] To the best of the authors' understanding of the guideline document, information presented is illustrative and not exhaustive.

First-Line Pharmacologic Treatment

There is unanimous agreement that intramuscular epinephrine [adrenaline] injected into the anterolateral thigh is first line treatment for anaphylaxis. The dose of epinephrine is generally consistent across guidelines: 0.01 mg/kg of body weight using a 1 mg/ml (1:1000) dilution, with maximum single doses of 0.3-0.5 mg for adults, 0.3 mg for older children, and 0.15 mg for younger children. These dosages can be repeated every 5 to 15 minutes if symptoms persist or worsen. This international consensus is supported by clinical experience and observational data, which finds that delayed administration of epinephrine is a key risk factor for fatal outcomes. Of note, the EAACI guideline suggests that an epinephrine auto-injector (EAI) should be considered as a preferred alternative to injection by needle/syringe.[21]

Supportive and Adjunctive Management

Supportive and adjunctive interventions include intravenous (IV) crystalloid fluids for patients with hypotension or shock, particularly when unresponsive to initial epinephrine administration. Typical bolus volumes are 10 to 20 mL/kg in children and 500 to 1000 mL in adults. High-flow supplemental oxygen is universally recommended to address hypoxia.

Nebulized short-acting beta2-agonists, such as salbutamol, are often used as adjuncts for bronchospasm. However, guidelines strongly caution that these agents must not replace or delay epinephrine administration.

For patients taking beta-blockers with an inadequate response to epinephrine, due to persistent hypotension or bronchospasm, glucagon is consistently identified as a potential adjunctive treatment.

Antihistamines (H1 and sometimes H2 antagonists) and CS are considered second-line treatments. Antihistamines (AH) may relieve cutaneous symptoms. While CS are often used to prevent protracted or biphasic reactions, there is no evidence to support this recommendation. For instance, the RCUK guidelines clearly state that AH are a third-line option and CS are no longer recommended as part of emergency management.

Post-Acute Care and Long-Term Management

After the acute episode has been managed, guidelines consistently advocate for key elements of post-acute care and long-term risk reduction. Due to the risk of a biphasic reaction, guidelines recommend a period of observation following initial symptom

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resolution. The duration varies (eg, 4 to 6, 6 to 8, or 12 to 24 hours), depending on the severity of the reaction, need for repeat epinephrine, and/or presence of comorbidities such as asthma.

There is also strong agreement on comprehensive patient education and access to epinephrine, which can reduce morbidity and mortality. Education should include trigger avoidance, symptom recognition, the immediate use of epinephrine, and how to utilize a personalized emergency action plan (EAP). The prescription (1 or 2) and education on the use of EAIs are universally supported. Some guidelines or local adoption refer to carrying epinephrine solution and a syringe when registered EAIs are unavailable in their country.

Referral to an allergy specialist is widely endorsed to confirm the diagnosis, identify triggers, provide education on avoidance strategies and management, and recommend allergen immunotherapy (AIT), when appropriate. Guidelines encourage health care systems to fund anaphylaxis educational programs and to offer affordable EAIs.

In summary, the international guideline consensus on anaphylaxis management signals a shift from reactive emergency care, for example, episodic, crisis-driven acute management, to a proactive model of risk stratification, patient and caregiver education, personalized EAPs, prophylactic strategies, and health care system readiness. **Table 3** summarizes the core recommendations where there is substantial agreement across the reviewed international anaphylaxis guidelines, highlighting the foundational elements of best practice in anaphylaxis care.

ANAPHYLAXIS MANAGEMENT: AREAS OF DISAGREEMENT

While different guidelines suggest different approaches to diagnosing anaphylaxis, there are minimal differences between guidelines concerning acute management, for example, in the precise dosage thresholds for EAIs based on body weight, or the recommended duration of post-reaction observation. Such variations typically reflect regional contexts, differences in health care infrastructure, or differing interpretations of the evidence in areas where data are limited or inconclusive. **Table 5** summarizes the key differences in anaphylaxis management in 9 of the international guidelines.

Some guidelines suggest that EAIs[21] can be used for initial management—even in hospital settings—while the RCUK guideline also cautions that EAIs should only be used for the first dose due to concerns over negative inotropy. When patients do not respond to the first dose of epinephrine, a further dose should be administered after at least 5 minutes. Guidelines differ in terms of the window in between further doses, with some suggesting 5 minutes and others providing a 5 to 15 minute window.

While most guidelines discuss adjuvant treatment, more recent guidelines stress the adjunctive, not primary, role of AH and/or CS to manage acute anaphylaxis and are equivocal about their routine use. Most discuss the use of IV fluids to support the circulation, although in children, there is a lack of consensus as to whether the volume administered should be 10 mL/kg or 20 mL/kg.

The more recent guidelines also discuss when treatment should be escalated, although only the RCUK guideline has a specific algorithm for refractory anaphylaxis. The ASCIA guideline specifically cautions that “Infants with anaphylaxis may retain pallor despite 2-3 doses of adrenaline, and this can resolve without further doses. More than 2-3 doses of adrenaline in infants may cause hypertension and tachycardia, which is often misinterpreted as an ongoing cardiovascular compromise or anaphylaxis.”

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Table 5
Differences in international anaphylaxis guidelines

	Diagnosis	Initial Treatment	Adjuncts	Refractory Reactions	Observation & Discharge	Serum Tryptase	Comments
EAACI	NIAID/FAAN 2006. ABC approach also discussed.	Recommends EAI for initial dose, repeat after 5–10 min	O2, neb epi, salbutamol. Equivocal re AH, GCT Fluids: 10 mL/kg–500 mL	Defined as ongoing features despite 2 doses of epi and IV fluids	Based on JTFPP 2020: 6-8h for respiratory compromise, 12–24 h if hypotension present. Includes guidance on EAI prescription.	If measured, to be done 30–120 mins after onset.	
RCUK	ABC approach	IM syringe (AAI can be used), repeat after 5 min	No AH, GCTs Fluids: 10 mL/kg–1 L	Defined as ongoing features despite 2 doses of epi. Includes a separate algorithm	2 hrs acceptable for straightforward cases, otherwise overnight.	Measure in all patients where the diagnosis is uncertain, blood sample to be taken within 2–4 h.	
JTFPP 2023	Preference for NIAID/FAAN 2006. Specifically flags that diagnosis in infants can be challenging.				Includes guidance on EAI prescription.	Assess baseline tryptase in patients with recurrent, idiopathic, or severe anaphylaxis (especially hypotension). Acute samples within 2 h of onset.	Not strictly a guideline. Includes evidence relating to community management, including when to contact EMS

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Table 5
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	Diagnosis	Initial Treatment	Adjuncts	Refractory Reactions	Observation & Discharge	Serum Tryptase	Comments
NICE	ABC approach				6–12 h from onset, overnight in children <16 y. A shorter observation period may be considered in adults with non-complicated reactions.	Measure in all patients >16 y, ideally within 1–2 h of onset. <16, measure where the cause is thought to be venom-related, drug-related or idiopathic	Not a full guideline
WAO 2020	WAO 2020 criteria	IM syringe (AAI can be used), repeat every 5–15 min	O2, neb epi, salbutamol. Limited role for AH, GCT; routine use of GCT is no longer recommended Fluids: 20 mL/kg–1 L	No specific definition	Patients need to be observed, especially after a severe reaction/ requiring multiple epi doses	Tryptase can help provide diagnostic clarity after the event, but no specific recommendations.	
Germany	NIAID/FAAN 2006, though ABC approach mentioned with respect to ICU management	IM syringe (AAI can be used), repeat every 5–10 min	O2, neb epi, salbutamol. Fluids: 20 mL/kg to 1L Limited role for AH, GCTs	Failure to stabilize: iv epinephrine boluses, 1 ug/kg	Includes recommendations re who to prescribe EAI to.	Tryptase (1–3 h post) can be helpful	Standard maximum dose of IM adrenaline is 0.5 mg; however, the mathematical upper limit of weight-based dosing is 0.6 mg

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GA2len	New consensus criteria. Infants may present with distinct signs.	IM, give every 5–15 min	Must not delay IM epi	Failure to respond to 2 doses. IV epi infusion preferred over bolus		May be helpful	Not a guideline
ASCIA	WAO 2020 criteria	IM syringe (AAI can be used), repeat after 5 min	O2, neb epi, salbutamol. Fluid: 20 mL/kg–1 L Limited role for AH, GCTs	Consider epi infusion if multiple (2–3) doses ARE needed or if the patient deteriorates	4 h minimum	Not mentioned	
Canadian Paed. Society	NIAID/FAAN 2006	Repeat every 5–15 min	O2, neb epi, salbutamol. Fluid: 20 mL/kg AH, GCT 2nd line	Hypotension despite persistent fluid boluses	4–6 h		

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MAJOR KNOWLEDGE GAPS IN THE DIAGNOSIS AND MANAGEMENT OF ANAPHYLAXIS

Knowledge gaps in the diagnosis and treatment of anaphylaxis impede the clinician's ability to manage their patients effectively.[22] There is a lack of global consensus on the exact anaphylaxis diagnostic and management; this would transform care from the one-size-fits-all model to a precision medicine model that accounts for causative agents, the susceptibility, and the response of the host.[23] Underreporting of anaphylaxis episodes leads to a gap in epidemiologic data. Studies using emergency department data alone miss cases treated in other facilities and prehospital actions.[24]

Physicians' Knowledge Deficits

Case series consistently show that under 20% of anaphylaxis episodes are treated with epinephrine, whether by patients/first-responders or even emergency departments.[4] In many global health care facilities, epinephrine is replaced by other therapies such as AH and systemic CS, for which there are insufficient data to support their use.[25] However, premedication with AH and/or CS may be of value for rush, and, sometimes, for conventional AIT, radio-contrast imaging, chemotherapy, and surgery after perioperative anaphylaxis (POA)[22] but validated algorithms on the use of these medications in the context of anaphylaxis are needed.

Survey data indicate that many physicians believe there are contraindications to epinephrine use and do not know the correct dose when prescribing epinephrine ampoules.[26] Medical residents and interns often have knowledge gaps in diagnosing and managing drug allergy, for example, as the benefits and limitations of using laboratory testing to confirm drug-induced anaphylaxis.[27] No evidence-based data exists on the proper dose of IV titrated epinephrine or the need for fluid therapy in POA. There is also a lack of data supporting the administration of second-line drugs such as glucagon and methylene blue. In addition, there is a knowledge gap due to the limited research focused on identifying novel biomarkers that could signal when additional interventions are warranted.[28]

Parents/Caregivers' Knowledge Gaps

In a study involving parents of 624 children with anaphylaxis, mothers reported greater empowerment compared with fathers in the management of anaphylaxis, emphasizing that the entire family must be engaged in anaphylaxis education.[29] For many parents, managing an acute anaphylactic reaction is frightening and stressful, mainly due to the unpredictability and uncertainty of the responses. These feelings are often related to knowledge gaps about anaphylaxis management, underscoring the need for practical resources for parents. Many parents prefer to be instructed by the health care providers in writing, and in plain language that is easy to understand and follow.[30]

Gaps in Preschool and School Settings

Anaphylaxis does occur in infants and preschoolers, particularly due to food, and yet there are no consistent food allergy management practices in early learning and childcare centers. Early childhood educators are expected to manage and prevent food allergy reactions, but their training is variable across nations and centers. Strategic guidance implementation may be beneficial in this setting and can engage all stakeholders, including parents. Periodic education and availability of EAIs and AEPs are necessary for effective management of anaphylactic reactions in early life care centers.[31]

In-school management of food allergies is highly variable. A study of allergic reactions and food allergy-related bullying in elementary school teachers revealed that

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Table 6
The most common knowledge gaps in the diagnosis and management of anaphylaxis

Gaps in the Diagnosis	Gaps in the Management
1. Definition and diagnostic clinical criteria for global use	1. Validation of the use of vasopressin and methylene blue for refractory POA
2. A separate set of clinical criteria for diagnosing anaphylaxis in infants and non-verbal or minimally verbal populations and in POA	2. Validation of the use of albumin and colloids for hypotension refractory to crystalloid during POA
3. Definition and criteria based on observable symptoms without requiring physiological measurements or medical examination	3. Benefit of premedication with the same or alternative perioperative agent(s) with and without diagnostic testing/challenge
4. Point-of-care criteria for administering epinephrine during a severe allergic reaction and/or evolving anaphylaxis	4. Treatment algorithm for selecting perioperative agent(s) for future surgery after POA, with and without diagnostic testing/challenge
5. The validity of epinephrine usage and the observed clinical response as a surrogate marker	5. Algorithm for determining an individual patient's ED observation time based on a risk/benefit assessment
6. A validated global severity scoring system	6. Time (max) and concentration (max) for epinephrine injection with site confirmed by ultrasound
7. The best biomarker to diagnose/confirm anaphylaxis and predict the severity of future reactions	7. Guidelines for IV vs IM epinephrine using risk/benefit assessment
8. Validated tools for diagnosing HαT and mastocytosis in patients with IA	8. Global consensus on ideal dose and needle length of EAI in infants, children, and adults
9. Validation of TSAB1 copy number in conjunction with bST to determine the need for a clonal mastocytosis workup in patients with IA	9. Risk of intraosseous injection in infant based on needle length and adverse events
10. Validation of the bST value for which a peripheral blood *KIT* D816 V mutation should be tested	10. Point-of-care, patient-friendly, guide, and action plan for using epinephrine when an allergic reaction is suspected.
11. Validation of screening patients with venom hypersensitivity for mastocytosis	11. Risk stratification aids in considering trigger, cofactors, and comorbidities for deciding how many EAIs to prescribe
12. Improved data collection of anaphylaxis/severe allergic reactions from all health care facilities including the location, trigger, symptom onset and evolution, cofactors, comorbidities, initial and subsequent treatment by location, and outcomes	12. Guidance for health care professionals and patients in deciding if and when to give epinephrine
13. Clinical algorithm for use at point of care to diagnosis of POA	13. Validated ways to prevent accidental injury from EAIs
14. Positive and negative likelihood ratios for skin and challenge testing for agents potentially responsible for POA	14. Validated ways to reduce the underuse of epinephrine for anaphylaxis
15. Optimal timing for skin testing and challenge after POA	15. When to introduce IV fluids and oxygen in the treatment of anaphylaxis
16. The cross-reactivity of alternative/similar pharmacologic agents for use during surgery	16. Role of H1 and H2 AH and CS in the prevention of anaphylaxis, for example, allergen immunotherapy, radiocontrast agents, chemotherapy, surgery after POA, and IA
17. Access to all pharmacologic agents used during surgery and alternative agents' determination for future use	17. How the timing of epinephrine and supplemental treatments affect the mechanisms responsible for anaphylaxis
	18. Evidence-based treatment algorithm for idiopathic anaphylaxis

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Table 6
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Gaps in the Diagnosis	Gaps in the Management
18. Validation of high sensitivity sIgE and BAT to identify agents responsible for POA 19. Predictive values of positive-graded and negative-graded challenges for agents potentially responsible for POA 20. Definition of biphasic, refractory, and persistent anaphylactic reactions 21. Validation of risk factors for biphasic anaphylaxis 22. Is there a requirement for epinephrine administration during initial anaphylaxis before diagnosing biphasic anaphylaxis? 23. What treatment is required before fulfilling the definition of refractory and persistent anaphylaxis?	19. Incidence of BB-related and ACEI-related severe and treatment-refractory anaphylaxis in immunotherapy, drug desensitization, IA, mast cell disorders, food allergy, and drug allergy 20. Selective vs nonselective BB and ACEI vs ACE receptor blockers as anaphylaxis risk factors 21. Do BB/ACEI complicate the treatment of anaphylaxis, for example, increased epinephrine dosage and need for glucagon 22. Evidence-based algorithm for discussing with a patient the risk/benefit of using BB/ACEI 23. Cost-effectiveness of unassigned EAI in community settings 24. The best content, format, delivery method, and frequency of training programs to achieve best outcomes 25. Role of patient-worn allergen identifiers, for example, Medi-Alert jewelry 26. Value of sublingual and intranasal epinephrine after marketing 27. Need for generic and patient-specific AEP with patient-friendly terminology that are valid on a global level 28. Components of the AEP, for example, benefit vs risk of including AH and its timing and indications and signs and symptoms that indicate that epinephrine should be administered 29. Evidence-based position statement on school food bans and allergy-free tables 30. Algorithm for physician/patient shared decision-making of when to activate EMS after the use of an EAI by patient at home/work 31. The format, content, and ideal frequency of clinician-provided patient-specific anaphylaxis education and the best method to provide anaphylaxis education in community settings, for example, restaurants, schools, and camps 32. Patient education and EAP should be consistent with the individual's racial, cultural, and socioeconomic background 33. Validated assessment of the psychological impact of anaphylaxis diagnosis and treatment on the patient and caretakers

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AEP, anaphylaxis emergency plan; BAT, basophil activation test; BB, beta-blocker; bST, baseline serum tryptase; EAI, epinephrine auto-injector; EMS, emergency medical services; HαT, hereditary alpha tryptasemia; IA, idiopathic anaphylaxis; *KIT* D816V: POA, perioperative anaphylaxis; sIgE, serum specific IgE; TSAB1, tryptase alpha/beta1.

Adapted from Wallace DV, 2023.[22]

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many factors influence their decision-making. Teachers consider the individualized needs of their students and rely on families for support. They requested more training and resources to enhance their food allergy and anaphylaxis management skills, including EAI administration and usage of AEP.[31]

Unmet Needs in Anaphylaxis Education

Although national, regional, and international guidelines all recommend written AEP, they rarely endorse a specific plan nor identify the particular components that should be included.[22] It has been reported that only 39% of patients diagnosed as being at risk of anaphylaxis possess a written AEP.[32] A consensus exists that patients benefit from the clinician-provided instructions on anaphylaxis management; however, the content and frequency of these educational sessions have yet to be determined.[22] Finally, all educational efforts must be consistent with the patient's/caregiver's ethnic, cultural, and socioeconomic background.[22] The most common knowledge gaps in anaphylaxis diagnosis and treatment are briefly presented in **Table 6**.

SUMMARY

This comparative analysis of 12 contemporary anaphylaxis guidelines reveals both progress and persistent challenges in achieving international harmonization. Since 2006, there has been growing adoption of GRADE methodology for evidence evaluation and increased stakeholder involvement, including patients and advocacy groups. However, most recommendations remain consensus-based, reflecting the scarcity of high-certainty evidence. While the foundational recommendation of prompt intramuscular epinephrine is universally endorsed, notable variations exist in diagnostic criteria, post-acute care duration, and the role of adjunctive therapies. The heterogeneity of definitions and criteria—particularly for infants and in patients without cutaneous symptoms—has contributed to delays in recognition and treatment.

The transition from reactive, acute, crisis-driven care to proactive risk reduction models shows promise, but implementation remains inconsistent. Regional differences in health care delivery, including the lack of affordable AAI in many countries, and inconsistent application of educational strategies, create gaps in optimal management. Particularly concerning is the persistent underuse of epinephrine, the inappropriate reliance on corticosteroids and antihistamines, and limited clinician and caregiver knowledge regarding anaphylaxis recognition and response.

Global harmonization of definitions and treatment algorithms, while retaining flexibility for local adaptation, is urgently needed. Future research must prioritize validated diagnostic criteria, standardization of EAPs, and outcomes-focused educational interventions across all settings—including early childhood centers and schools. The development of patient-centered tools, incorporation of stakeholder input, and the application of equity-based frameworks are essential to reduce disparities and improve outcomes.

Until more robust data emerge, clinicians must rely on guideline-informed judgment, emphasizing rapid epinephrine use, appropriate observation, and post-episode referral. Improving anaphylaxis care will require coordinated efforts among guideline developers, educators, clinicians, and policymakers.

CLINICS CARE POINTS

Clinical Pearls

- *First-Line Treatment*: Administer intramuscular epinephrine (0.01 mg/kg, max 0.5 mg) promptly upon suspicion of anaphylaxis.

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- *Observation Duration*: Patients requiring multiple doses of epinephrine or presenting with severe anaphylaxis should receive extended observation of up to 6 hours or longer due to the risk of biphasic reactions.
- *Adjunctive Medications*: While antihistamines and corticosteroids are commonly used, they are second-line therapies and have not been shown to prevent biphasic anaphylaxis.
- *Education and Follow-Up*: All patients should receive education on anaphylaxis, trigger avoidance, and proper use of EAIs. Referral to an allergist for follow-up evaluation is recommended.

Common Pitfalls
- *Misdiagnosis*: Do not dismiss anaphylaxis in the absence of skin symptoms as 10% to 20% of cases may lack urticaria or rash.
- *Delayed Epinephrine Use*: Avoid postponing epinephrine administration in favor of other treatments; delays in epinephrine administration are associated with increased morbidity and mortality.
- *Inadequate Observation*: Discharging patients too early, especially those with severe presentations or multiple epinephrine doses, increases the risk of undetected biphasic reactions.
- *Overreliance on Adjuncts*: Relying solely on antihistamines or corticosteroids without epinephrine can lead to worsening symptoms and delayed recovery.

DISCLOSURES

D.V. Wallace: On advisory boards of ARS, Bryn, Genetech, Grisfols, Kaleo. Author on the JTFPP guidelines on anaphylaxis and past co-chair of the JTFPP. P.J. Turner: P.J. Turner declares grants from the UK Food Standards Agency, Jon Moulton Charity Trust, United Kingdom; NIHR/Imperial Biomedical Research Centre, United Kingdom; Medical Research Council, United Kingdom, outside the submitted work; personal fees from UK Food Standards Agency, UpToDate, Elsevier, ALK, and Allergenis outside the submitted work. P.J. Turner is also the current chair of the WAO Anaphylaxis Committee and co-lead of the Resuscitation Council UK Anaphylaxis Working Group. E.M. Hossny, M. Levine, and D. Munblit have nothing to disclose.

REFERENCES

1. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report–Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol 2006;117(2):391–7.
2. Golden DBK, Wang J, Waserman S, et al. Anaphylaxis: a 2023 practice parameter update. Ann Allergy Asthma Immunol 2024;132(2):124–76.
3. Muraro A, Worm M, Alviani C, et al. EAACI guidelines: anaphylaxis (2021 update). Allergy 2022;77(2):357–77.
4. Ring J, Beyer K, Biedermann T, et al. Guideline (S2k) on acute therapy and management of anaphylaxis: 2021 update: S2k-Guideline of the German Society for allergology and clinical immunology (DGAKI), the Medical Association of German allergologists (AeDA), the Society of pediatric allergology and environmental medicine (GPA), the German academy of allergology and environmental medicine (DAAU), the German professional Association of pediatricians (BVKJ), the Society for neonatology and pediatric intensive care (GNPI), the German Society of dermatology (DDG), the Austrian Society for allergology and immunology (OGAI), the Swiss Society for allergy and immunology (SGAI), the German Society of anaesthesiology and intensive care medicine (DGAI), the German Society of

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pharmacology (DGP), the German respiratory Society (DGP), the patient organization German allergy and Asthma Association (DAAB), the German working Group of anaphylaxis training and education (AGATE). Allergo J Int 2021;30(1):1–25.
5. Russian Association of Allergologists and Clinical Immunologists FoAaR. Анафилактический шок: клиническая рекоМендация (2-й пересМотр) [anaphylactic shock: clinical guideline (2nd revision)]. Available at: https://www.algom.ru/post/nkr00263-Anafilakticheskii_shok__2025_g__(odobreno_NPS_MZ_RF)?lang=rus. Accessed June 7, 2025.
6. Working Group of Resuscitation Council UK. Emergency treatment of anaphylaxis Guidelines for healthcare providers. Resuscitation Council UK. Available at: https://www.resus.org.uk/sites/default/files/2021-05/Emergency%20Treatment%20of%20Anaphylaxis%20May%202021_0.pdf. Accessed June 7, 2025.
7. National Institute for H, Care E. Anaphylaxis: assessment and referral after emergency treatment for a suspected anaphylactic episode. NICE Clinical Guideline; 2011. Available at: https://www.nice.org.uk/guidance/cg134.
8. National Institute for H, Care E. Anaphylaxis: assessment and referral after emergency treatment. NICE Clinical Guideline; 2016. Available at: https://www.nice.org.uk/guidance/cg134.
9. National Institute for Health and Care Excellence. Anaphylaxis. Available at: https://www.nice.org.uk/guidance/qs119. Accessed June 7, 2025.
10. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. World Allergy Organ J 2020;13(10):100472.
11. ASCIA. Acute management of anaphylaxs. 2024. Available at: https://www.allergy.org.au/hp/papers/acute-management-of-anaphylaxis-guidelines. Accessed January 27, 2025.
12. Japanese Society of Allergology AC. アナフィラキシーガイドライン 2022 [Anaphylaxis Guideline 2022]. Japanese Society of Allergology. Available at: https://www.jsaweb.jp/uploads/files/Web_AnaGL_2023_0301.pdf. Accessed June 7, 2025.
13. Dribin TE, Muraro A, Camargo CA Jr, et al. Anaphylaxis definition, overview, and clinical support tool: 2024 consensus report-a GA(2)LEN project. J Allergy Clin Immunol 2025;155(2):300–12.
14. Canadian Paediatric Society AWG. Emergency treatment of anaphylaxis in infants and children. Paediatr Child Health 2018;16(6):381–5.
15. Allergy ASoCIa. ASCIA Guidelines - Acute management of anaphylaxis. Available at: https://www.allergy.org.au/images/ASCIA_HP_Guidelines_Acute_Management_Anaphylaxis_2024.pdf. Accessed June 7, 2025.
16. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report–second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Ann Emerg Med 2006;47(4):373–80.
17. Anaphylaxis: assessment and referral after emergency treatment (2021).
18. Turner PJ, Worm M, Ansotegui IJ, et al. Time to revisit the definition and clinical criteria for anaphylaxis? World Allergy Organ J 2019;12(10):100066.
19. Public Health O. Management of anaphylaxis following immunization in the community. 2022. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/vaccines/2021/03/managing-anaphalaxis-following-immunization.pdf?la=en.
20. Barniol C, Dehours E, Mallet J, et al. Levocetirizine and prednisone are not superior to levocetirizine alone for the treatment of acute Urticaria: a randomized double-blind clinical trial 2018;71(1):125–31.e1. https://doi.org/10.1016/j.annemergmed.2017.03.006.

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21. Patoux-Pibouin M, Beneton C, Delaval Y, et al. Sucralfate (Ulcar® granules) as an inducer of anaphylactoid reaction? [2]. 1993;3(6):506–7.
22. Wallace DV. Knowledge gaps in the diagnosis and management of anaphylaxis. Ann Allergy Asthma Immunol 2023;131(2):151–69.
23. Dribin TE, Schnadower D, Wang J, et al. Anaphylaxis knowledge gaps and future research priorities: a consensus report. J Allergy Clin Immunol 2022; 149(3):999–1009.
24. Stiles SL, Sanfilippo FM, Murray K, et al. Investigating health care pathways for anaphylaxis: seeing the bigger picture through linked data. J Allergy Clin Immunol Glob 2025;4(1):100371.
25. Dribin TE, Castells M. Anaphylaxis: data gaps and research needs. Immunol Allergy Clin North Am 2022;42(1):187–200.
26. Pimentel-Hayashi JA, Navarrete-Rodriguez EM, Moreno-Laflor OI, et al. Physicians' knowledge regarding epinephrine underuse in anaphylaxis. Asia Pac Allergy 2020;10(4):e40.
27. Gokmirza Ozdemir P, Kizilca O, Aylanc H, et al. Residents and interns in the 3 university hospitals: their knowledge of and attitudes to drug allergy. Asia Pac Allergy 2020;10(3):e31.
28. Pouessel G, Tacquard C, Tanno LK, et al. Anaphylaxis mortality in the perioperative setting: epidemiology, elicitors, risk factors and knowledge gaps. Clin Exp Allergy 2024;54(1):11–20.
29. Warren CM, Gupta RS, Sohn MW, et al. Differences in empowerment and quality of life among parents of children with food allergy. Ann Allergy Asthma Immunol 2015;114(2):117–25.
30. Rahman S, Elliott SA, Scott SD, et al. Children at risk of anaphylaxis: a mixed-studies systematic review of parents' experiences and information needs. PEC Innov 2022;1:100018.
31. Santos MJL, Merrill KA, Ben-Shoshan M, et al. Food allergy education and management in early learning and childcare centres: a scoping review on Current practices and gaps. Children (Basel) 2023;10(7). https://doi.org/10.3390/children10071175.
32. Simons FE, Clark S, Camargo CA Jr. Anaphylaxis in the community: learning from the survivors. J Allergy Clin Immunol 2009;124(2):301–6.

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